

Amendments to the Drawings:

Please delete Figure 8.

II. REMARKS

A. Introduction

Applicants submit this Response in a bona fide attempt to (i) advance the prosecution of this case, (ii) answer each and every ground of objection and rejection as set forth by the Examiner, (iii) place the claims in a condition for allowance, and (iv) place the case in better condition for consideration on appeal. Applicants respectfully requests reexamination and reconsideration of the above referenced patent application in view of this Response.

As indicated above, Applicants have amended Claims 1-3 and canceled Claims 7, 8, 10 and 11. New Claims 46-52 have also been added.

In accord with the Examiner's request, the alleged new matter submitted on July 15, 2004 has also been deleted.

Applicants respectfully submit that the noted amendments and added figure merely make explicit that which was (and is) disclosed or implicit in the original disclosure. The amendments and new figure thus add nothing that would not be reasonably apparent to a person of ordinary skill in the art to which the invention pertains.

B. Response to Objections

The Examiner has objected to the amendment filed on July 15, 2004. The Examiner contends that the amendment "introduces new matter into the disclosure". Applicants have accordingly deleted the matter at issue from the application.

C. Response to Rejections

The Examiner has rejected Claim 8 under 35 USC § 103(a) as being unpatentable over Theeuwes et al. (WO 98/28037). As the Examiner notes, Theeuwes et al. discloses a method of delivering or sampling glucose through the stratum corneum with a microprotrusion member, forming microslits and delivering or sampling glucose through the microslits.

The Examiner admits that the Theeuwes et al. does not disclose impacting the stratum corneum with a power of at least 0.05 joules per cm² in 10 milliseconds or less. However, the Examiner has concluded that "it would have been an obvious matter of design choice to a person of ordinary skill in the art to impact the stratum corneum with a power of at least 0.05 joules per cm² of the microprotrusion member in 10 milliseconds or less because Applicants have not

disclosed that this measurement provides an advantage, is used for a particular purpose, or solves a stated problem.”

Although Claim 8 has been canceled, the Examiner’s conclusion is equally applicable to Claim 1, as amended, and new Claim 47, dependent thereon. Applicants will thus respond accordingly.

Applicants submit that the specification, as filed, does indeed disclose multiple benefits associated with applying the microprotrusion member by impacting the stratum corneum with the specific claimed energy. Indeed, as attested to by Dr. Robert T. Stone, the specification clearly discloses that applying the microprotrusion member to the stratum corneum with the claimed impact energy (i.e., application parameters) provides several significant, stated advantages, is used for at least one stated purpose and solves at least one stated problem. (see **Declaration of Dr. Robert T. Stone, ¶ 6, filed concurrently herewith**).

The specification page 5, in paragraph 13, teaches that the applicator device delivers sufficient power for effective penetration of the stratum corneum. The specification on page 9 next provides that “impact spring 20 is also preferably selected to achieve the desired skin penetration without exceeding an impact which causes discomfort to the patient”. The specification additionally provides that the “impact spring 20 is preferably selected to deliver a minimum amount of energy of 0.05 Joules per cm², which is delivered in less than 10 milliseconds (msec).” Thus, the specification clearly teaches that using the claimed impact energy results in the benefit of creating uniform, effective penetration of the stratum corneum without undue patient discomfort. (see **Stone Decl., ¶ 7**)

This teaching is reinforced by Examples 1 and 2, page 12-14, paragraphs 41-44, which compare the use of an impact applicator that utilizes the claimed amount of energy in the specified time to manual application. These examples demonstrate that application of the microprotrusion member with the claimed power parameters results in an additional benefit and, hence, advantage of increased rate of agent delivery. This is *clearly* a benefit and, hence, stated advantage associated with applying the microprotrusion member by impacting the stratum corneum with the claimed energy. (see **Stone Decl., ¶ 7**)

Applicants further submit that the specification discloses that applying the microprotrusion member in the claimed manner solves a specific problem, i.e., inconsistent application. As is well known in the art, prior art means of applying a microprotrusion member

typically result in “significant variation in puncture depth across the microprotrusion array” and in “large variations in puncture depth between applications.” (see **Stone Decl.**, ¶ 8) As is clearly set forth in the specification, using the claimed energy parameters to apply a microprotrusion member to the stratum corneum achieves the particular and stated purpose of creating effective, uniform and consistent penetration of the stratum corneum, which is not taught or suggested by any prior art reference. (see **Stone Decl.**, ¶¶ 7, 8 and 12).

For example, the specification on pages 2-3, paragraph 6, unequivocally provides that it is desirable to effect “consistent, complete and repeatable penetration of the skin.” The specification on page 3, paragraph 8, further provides that the present invention solves the problems of inconsistent and incomplete penetration of the skin by causing “the microprotrusion member to impact the stratum corneum with a certain amount of impact determined to effectively pierce the skin with the microprotrusions.”

In contrast, as the Examiner admits, Theeuwes et al. does not disclose or suggest the use of the claimed impact parameters. Indeed, Theeuwes et al. does not disclose any specific means of applying the microprojection member.

Further, as attested to by Dr. Stone, Theeuwes et al. neither provides teaching that would allow one having skill in the art to apply a microprojection member to the stratum corneum with the claimed energy in the specified time, nor motivate one to do so to realize the advantages set forth herein. Indeed, none of the cited references, alone or in combination, recognize the problems solved by Applicants’ claimed application parameters or even suggest an energy of application. (see **Stone Decl.**, ¶ 9)

Applicants additionally submit that Applicants’ experimental results contradict the Examiner’s conclusion that “one of ordinary skill in the art, furthermore, would have expected Applicants’ invention to perform equally well with either the measurement taught by Theeuwes or the claimed measurement.” Applicants’ experimental results clearly reflect that a microprotrusion member applied to the stratum corneum with the claimed impact energy provides enhanced transdermal delivery as compared to the manual application of a microprotrusion member, which is inherently taught by Theeuwes et al. (see **Stone Decl.**, ¶ 10)

Additionally, as set forth in Dr. Stone’s Declaration, a further benefit associated with the application of a microprotrusion member to the stratum corneum with the claimed impact energy accrues as a result of the hold-down spring force which optimally tensions the skin for the impact

driven penetration. It is the combination of the impact energy delivery, resultant impact velocity, residual force in the piston spring, tension of the skin (as maintained by the hold-down spring force required for actuation of the piston), which results in the optimum performance parameters described and claimed. This combination of parameters as an optimum is not obvious to one skilled in the art and would require extensive experimentation to determine. **(Stone Decl., ¶10)**

Applicants thus respectfully submit that Claim 1, and all claims dependant thereon, should be deemed allowable.

The Examiner has also rejected Claims 1-3, 7, 10 and 11 under 35 USC § 103(a) as being unpatentable over Theeuwes et al. (WO 98/28037), Effenhauser (WO 96/17648), Gerstel et al. (US 3,964,482), Gross et al. (US 5,279,544) and Godshall et al. (US 5,879,326). The Examiner contends that each of these references discloses a method of delivering or sampling glucose through the stratum corneum with a microprotrusion member, forming microslits and delivering or sampling glucose through the microslits. The Examiner concedes that the cited references do not disclose impacting the stratum corneum with a power of at least 0.05 joules per cm² in 10 milliseconds or less. However, the Examiner has again concluded that “it would have been an obvious matter of design choice to a person of ordinary skill in the art to impact the stratum corneum with a power of at least 0.05 joules per cm² of the microprotrusion member in 10 milliseconds or less because Applicants have not disclosed that this measurement provides an advantage, is used for a particular purpose, or solves a stated problem.”

As discussed above, Applicants submit that the specification, as filed, does provide a clear teaching that the claimed impact delivery parameters yield at least one stated, specific advantage, achieve at least one particular purpose and solve at least one stated problem. Indeed, multiple, significant benefits and, hence, advantages and problems that are overcome by the invention are clearly stated in the specification. **(see Stone Decl., ¶¶ 6-8, 11-12)** One significant and stated advantage is that applying a microprotrusion member to the stratum corneum with the claimed impact energy provides uniform and effective penetration of the microprotrusions into the stratum corneum. This solves the ‘stated’ problems of variable penetration of the microprotrusions and inconsistent application. **(see Stone Decl., ¶ 8)** As noted in Examples 1 and 2, the uniform and reproducible (or consistent) penetration afforded by the use of the claimed impact energy further provides improved transdermal delivery, as compared to the manual application disclosed in the prior art.

The Examiner also reiterated that one of skill would have expected equal performance with either the measurement taught by the cited references or the claimed measurement. This contention is expressly contradicted by Dr. Stone. (see **Stone Decl., ¶ 12**) Moreover, in the examples discussed above, a microprotrusion member applied with the claimed impact energy *clearly* provides improved delivery over the manually applied microprotrusion member inherently taught by the cited references. Applicants' invention thus represents a significant advantage over the delivery taught by the Examiner's cited art. (see **Stone Decl., ¶ 12**)

Applicants accordingly respectfully request that the Examiner withdraw the Section 103(a) rejection of Claims 1-3.

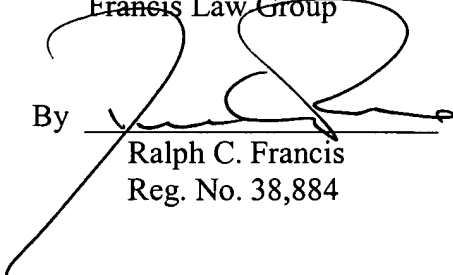
III. CONCLUSION

Applicants having answered each and every ground of objection and rejection as set forth by the Examiner, and having added no new matter, believe that this response clearly overcomes the reference of record, and now submit that all claims in the above-referenced patent application are in condition for allowance and the same is respectfully solicited.

If the Examiner has any further questions or comments, Applicants invite the Examiner to contact their Attorneys of record at the telephone number below to expedite prosecution of the application.

Respectfully submitted,
Francis Law Group

By


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